offer the greatest clinical difficulty. The absence of the Widal reaction, of the characteristic eruption and of the comparatively slow pulse in miliary tuberculosis, are to be especially noted. On the other hand, in cases in which strong suspicions of the existence of acute miliary tuberculosis are entertained, a careful search for tubercles in the choroid, and tubercle bacilli in the blood and sputum (if there be any), is to be carried forward. C. Loeb[1] has recently emphasized the value of ophthalmic examinations in the differential diagnosis between typhoid fever and acute miliary tuberculosis. The personal history is often most helpful. In doubtful cases an attempt should be made to cultivate the typhoid bacilli from any suspicious eruption that may be present. There are not a few cases in which a positive diagnosis, however, must be withheld, for lack of discriminating features.

DISTRIBUTION OF THE ULCERS IN TYPHOID FEVER.

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The occurrence of two cases of typhoid fever with an unusual distribution of the ulcers suggested the desirability of a general investigation of the distribution of ulcers in this disease. The two cases are presented in detail, and are followed by an analysis of a series of 89 cases, and by a review and discussion of the literature on the subject.

The first case showed ulcers in the œsophagus and colon, and in no other part of the alimentary tract:

Case I.—This series 33; Rush Medical series 945. A. B., male, aged twenty-four years; died January 31, 1901.

Clinical Diagnosis. Typhoid fever; tonsillitis; pharyngitis; laryngitis; pleuritis; probable pneumonia.

Anatomical Diagnosis (Dr. H. G. Wells). Typhoid fever (colotyphoid); ulcerative colitis; follicular enteritis; swelling of mesenteric lymph glands and spleen; follicular pharyngitis; œsophageal ulcers; acute serofibrinous pleuritis; bronchopneumonia; fibrous perisplenitis and perihepatitis; healed pulmonary tuberculosis.

Tongue. Lymphoid follicles prominent.

Pharynx and Epiglottis. Covered by mucopus.

Œsophagus. Covered by thin mucopus. There are prominent follicular swellings. At a point 1 cm. below the cricoid cartilage is a superficial ulcer 5 mm. in its long diameter, which is parallel to the axis of the œsophagus. Near this are three smaller ulcers; floor smooth, margins sharp, outline oval, long axis vertical.

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[1] Archives of Ophthalmology, New York, 1903, vol. xxxii. pp. 453–469.

Larynx and Trachea. Covered by thin mucopus. No ulcers.

Stomach. No ulcers.

Small Intestines. There is a slight hyperplasia of the solitary lymph follicles, especially in the lower part. Peyer's patches are normal. There is some hyperæmia. No ulcers.

Large Intestine. Beginning at a point 30 cm. below the ileocæcal valve and extending 70 cm. are twenty-five ulcers, 2 mm. to 6 mm. in diameter, with swollen, elevated edges. None have perforated. There is some hyperæmia and hyperplasia of the lymph follicles.

Bacteriology. The typhoid bacillus was isolated from the heart's blood and kidney.

In the second case the ulcers were limited strictly to the ascending and transverse colon, the sigmoid flexure, and rectum.

Case II.—This series 45; St. Luke's Hospital 38. E. T., male, aged twenty years; died and examined February 24, 1903.

Clinical Diagnosis. Typhoid fever; hypostatic pulmonary congestion; pseudohypertrophic muscular atrophy.

Anatomical Diagnosis (Dr. H. G. Wells). Typhoid ulceration of the colon; hypertrophic pulmonary emphysema; purulent bronchitis; bronchopneumonia, and left hypostatic pneumonia; œdema of the right lower lobe; acute lymphadenitis, peribronchial and mesenteric; hypoplasia of the aorta; hypertrophy of the left ventricle; parenchymatous degeneration of the liver and kidneys; fibrous pericholecystitis; atrophy of vermiform appendix; hyperplasia of the spleen; calcification of the peripancreatic and mesenteric lymph nodes; chronic diffuse nephritis; decubitus; hypoplasia of the testicles; fibrous increase in the thyroid; atrophy of the muscles of the lower extremities, with replacement by fatty fibrous tissue; contractures of the feet.

Œsophagus. The lymphoid nodules are prominent, but none are ulcerated.

Stomach. The mucous membrane is contracted, but the folds can be pulled out. No ulceration.

Duodenum. Lymphoid structures are prominent.

Lower Small Intestine. The last Peyer's patches are slightly swollen. A few irregular pigmented spots are found above the swollen Peyer's patches.

Large Intestine. Immediately below the ileocæcal valve is an ulcer 1 cm. in diameter. In the upper 30 cm. of the large bowel are five ulcers, the largest 2 cm. in diameter. There are also a few pigmented spots. 50 cm. below the valve are two ulcers, 1.5 cm. in diameter; 20 cm. farther another ulcer is found, 1 cm. in diameter; 35 cm. above the anus is an ulcer, 5 mm. in diameter; 10 cm. above the anus three ulcers are present, placed parallel, 3 cm., 2 cm., and 1 cm. in diameter, and transverse to the long axis of the bowel.

The series of 89 cases whose analysis is presented here was obtained from two sources, 44 cases from the Cook County Hospital, June, 1897, to June, 1903, and 45 cases from the Presbyterian Hospital, August, 1895, to July, 1902.

The distribution of the ulcers is as follows:

	Cases.	Percentage.
Mouth	0	0
Larynx	3	3.4
Trachea	1	1.1
Pharynx	0	0
Œsophagus	1	1.1
Stomach	2	2.2
Duodenum	0	0
Jejunum	1	1.1
Ileum	67	75.3
Ileum, lower half	32	35.9
Ileum alone	29	32.6
Meckel's diverticulum	1	1.1
Small intestine (not specific)	12	13.5
Total cases of involvement of small intestine	77	86.5
Ileocæcal valve	1	1.1
Vermiform appendix	1	1.1
Cæcum	15	16.9
Ascending colon	18	14.4
Transverse "	12	13.5
Descending "	5	5.6
Colon (not specific)	12	13.5
Sigmoid flexure	3	3.4
Rectum	3	3.4
Large intestine (not specific)	9	10.1
Large intestine alone	5	5.6
Cæcum alone	2	
Cæcum and ascending colon	1	
Cæcum and appendix	1	
Ascending colon, transverse colon, sigmoid flexure, and rectum	1	
Total cases of involvement of large intestine	45	50.6
No ulcers (with bacteriology)	2	2.2

Comparison of the percentages of distribution of the ulcers derived from this series with those derived from the general statistics in the literature, and which are presented later, reveals a close correspondence, except in two important items: In this series the percentage of involvement of the small intestine (in any part), 86.5 per cent., and of the ileum, 75.3 per cent., is markedly lower than the figures obtained from the older statistics, 99.4 per cent. and 89.9 per cent., respectively; while, on the other hand, the involvement of the large intestine in this series, 50.6 per cent., is more than double the percentage derived from other statistics—*i. e.*, 22.7 per cent.

This difference seems to me to indicate careful examination at the autopsies in this series, rather than variations that are the result of chance, and this explanation is further borne out by the fact that the same differences, though in less degree, exist between the earlier and the more recent statistics in the literature.

The bacteriology has been recorded in 37 of the 89 cases.[1] The typhoid bacillus, with or without other organisms, was found in 31 cases. Other organisms only were recovered in 6 cases.

Perforations were found in 14 cases (15.7 per cent.), distributed as follows: ileum, 9 cases (10.1 per cent.); cæcum, transverse colon, and large intestine, each 1 case (1.1 per cent.); and "vague," 2 cases. As is well known, the number of ulcers in typhoid fever varies considerably, and in this connection it is interesting to note that in one of these cases of perforation of the ileum the bowel presented but one ulcer, 30 cm. above the ileocæcal valve, and this solitary ulcer perforated, causing death by peritonitis.

Indeed, in recent years a large number of cases of typhoid fever entirely without ulceration has been reported. In this series there occur two such cases, and in both the bacteriology was carefully worked out, the typhoid bacillus being recovered and identified from the kidney, spleen, liver, and mesenteric lymph glands in one case, and from the kidney, spleen, and gall-bladder in the other case. This subject of typhoid fever without ulceration has been reviewed recently by Picchi, Bryant, Flexner and Harris, McPhedran and Ophüls. I have collected 26 cases, which, with the 2 cases in this series, make a total of 28 cases that seem to me to be valid on bacteriological grounds.[2] Search through the literature has yielded abundant data on the distribution of the ulcers in typhoid fever.

The material has been grouped in two divisions: first, a series of 83 individual cases, each involving unusual distribution of the ulcers; and second, a series of statistical analyses.

The 83 individual cases have been dissected below, in order to show the relative frequency of ulcerations in unusual sites:

		Cases.[3]	
Involvement of	larynx	17	
“ “	pharynx	16	
“ “	œsophagus	10	(4 are strictures)
“ “	trachea	1	
“ “	stomach	10	
“ “	jejunum	3	
“ “	Meckel's diverticulum	1	
“ “	appendix	5	
“ “	ileocæcal valve	3	
“ “	cæcum	12	
“ “	ascending colon	6	
“ “	transverse “	5	
“ “	descending “	4	
“ “	sigmoid flexure	3	
“ “	rectum	4	
“ “	skin at anus	1	
“ “	ileum and colon	12	(total 29)
“ “	small and large intestine (not specific)	17	
“ “	large intestine (alone)	6	

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[1] Sex: males, 66; females, 22; not given, 1. Age: twenty-one to thirty-five, 42; before twenty-one, 12; after thirty-five, 16; not given, 19 cases.

[2] Nine cases have been omitted because of a questionable bacteriology: 3 by Karlinski; 2 by Goodall; and 1 each by Banti, Thue, Guarnieri, and Dogliotti.

[3] In the appended bibliography all articles marked with an asterisk (*) contain one or more of these cases.

The general statistics from the literature have been dissected and rearranged on an anatomical basis, rather than a classification based on authorship, thus affording a more intelligible arrangement for comparative purposes. Under each anatomical division the average obtained from the data presented by the various authors is given first, followed by the result of the analysis of my series of 89 cases, and finally an average of the two totals, where both are given:

	Literature.		My series of 89 cases.	Average.
	Total cases.	Per ct.	Per ct.	Per ct.
Ulcers of mouth	......	......	....	none mentioned.
" larynx	1020	21.3	3.4	19.9
" trachea	439	0.2	1.1	0.38
" pharynx	648	2.5	...	2.2
" œsophagus	134	6.7	1.1	4.5
" stomach	1019	1.9	2.2	1.98
" duodenum	891	0.3	...	0.30
" jejunum	1269	6.1	1.1	5.9
" ileum	1334	89.9	75.3	89.0
" ileum (lower half)	316	37.0	35.9	36.8
" ileum (alone)	245	60.8	32.6	53.3
" Meckel's diverticulum	......	......	1.1	1.1
" common bile-duct	439	0.23	....	0.23
" small intestine (in any part)	534	99.4	86.5	97.5
" ileocæcal valve	......	......	6.7	6.7
" vermiform appendix	352	2.8	1.1	2.5
" cæcum	1307	31.3	16.9	30.3
" ascending colon	532	9.6	14.4	10.3
" transverse "	532	3.2	13.5	4.5
" descending "	532	2.1	5.6	2.6
" colon (not specific)	1092	29.1	....	29.1
" sigmoid flexure	12	33.3	3.4	6.9
" rectum	967	2.2	3.4	2.4
" large intestine	1084	22.7	50.6	33.3
" large intestine (alone)	......	......	5.6	5.6
No ulcers (with a bacteriology)	......	......	2.2	2.2

In reviewing the results obtained from a study of the literature, several facts worth noting are brought into prominence. Probably most striking among these is the wide distribution of the typhoid ulcers. They are found in every division of the alimentary tract, excepting the mouth, and they are found also in the larynx and trachea. One case has been reported by Mitchell, in which the observer speaks of a "loss of substance on each side of the tongue." No other mention of buccal involvement has been found.

Ulceration of the larynx in typhoid fever has been the occasion of much dispute, the point at issue being whether the lesion was due to typhoid bacillus or to fresh infections with pyogenic organisms (Kanthak and Drysdale, G. Duffy). Williams, in 1894, recovered the typhoid bacillus from the laryngeal ulcers in 2 cases, and since then the tendency has grown to regard these ulcers as primarily typhoidal. As long ago as 1829 Louis said: "The rarity of ulceration of the larynx is the more remarkable since ulcerations are frequently met with around that organ at the epiglottis, pharynx, and œsophagus. If laryngeal ulcers are found on a body dead of an acute disease, they will establish with nearly perfect certainty, and without going any farther, that the affection was typhoid fever."

Ouskow has analyzed the time of appearance of the ulcers in the larynx with these results: ulcers in the first week, none; in the second week, 79 cases; in the third week, 144 cases; in the fourth week, 89 cases.

The site of the ulcers, as determined by Lüning, in a series of 165 cases, was: supraglottic in 50 cases, infraglottic in 36 cases, and in the glottis in 18 cases. The author states that the process begins in the arytenoid cartilages and extends to the cricoid cartilages.

Ulceration of the trachea, while extremely rare, occurred in 3 cases in these statistics (Ouskow, Greffier, and this series).

Pharyngeal ulcers have been noted by many observers, and I have found 32 cases.[1]

Ulceration of the œsophagus, though found repeatedly by the earlier observers, Louis, Jenner, and Chomel, later became a rarity, as is strikingly shown by Packard's review of 5000 cases, none of which showed œsophageal ulceration. To a certain extent this negative result should be regarded as due to too brief a scrutiny or complete oversight on the part of the observer, for recently Mitchell, Riesman, and Pyle have presented a total of 10 cases (4 of which were strictures with recovery) and in this series there is another case (Case I.), which is given in detail because of the unique distribution of the ulcers, they being found only in the œsophagus and colon.

Gastric ulceration, though very unusual, is now regarded as quite possible in typhoid fever and may serve to explain some cases of hæmatemesis. In one of the 2 cases of gastric ulceration in this series the entire stomach has been preserved. Sections showed the ulcers to be fairly typically typhoidal, with numerous endothelioid phagocytic cells. In addition to 20 cases found in statistics,[2] a total of 10 individual cases is presented by Chauffard, Dignat, Perignon, and Keen.

The duodenum is the second rarest site for typhoid ulcers, only 3 cases being found. Two are by Louis and the third by Andral.

The low percentage of ulcers in the jejunum, 5.9 per cent., calculated from a total of 1358 cases, confirms the general impression as to the infrequency of jejunal involvement.

Involvement of the ileum is found in 89 per cent. of the cases; of the lower half of the ileum in 36.8 per cent., and of the ileum alone in 53.3 per cent. That typhoid ulcers elsewhere than in the ileum are found more commonly than has been supposed is demonstrated by the last percentage given, especially when this is viewed in connection with the high percentage of colonic involvement about to be presented.

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[1] Murchison, Moore, Osler, Ouskow, Roque, Derignac, Riesman.

[2] Murchison, Moore, Hawkins, and Andral.

Ulceration of the small intestine in any part has been recorded in 97.5 per cent. of 623 cases. Ulceration of Meckel's diverticulum has been noted twice, once in this series and once by J. Sailer.

Ulceration of the common bile-duct has been reported once by Ouskow in a series of 439 cases. This is the rarest site for typhoid ulcers. However, not only here but throughout all the statistics there is an element of doubt in the diagnoses. Perhaps it would be well to regard the ulcers as typhoidal only after recovery of the typhoid bacillus from the affected area and satisfactory demonstration of the histological picture shown by typhoid ulcers. The abrupt termination of the ulcer zone at the ileocæcal valve is well shown by the low percentage of involvement of the valve itself, 6.7 per cent.

The distribution of the ulcers in the large intestine has been considered under various captions. Involvement of the large intestine (without specification of locality) in 33.3 per cent. of 1173 cases, and of the colon in 29.1 per cent. of 1092 cases, only 65 of which are duplicates of the former number, is convincing evidence of the comparative frequency of ulceration in those sites. The division of the large intestine most frequently involved is the cæcum, 30.3 per cent. Next in order of frequency come: ascending colon, 10.3 per cent.; sigmoid flexure, 6.9 per cent.; transverse colon, 4.5 per cent.; descending colon, 2.6 per cent.; vermiform appendix, 2.5 per cent.; and rectum, 2.4 per cent.

Involvement of the large intestine alone was not found in any statistics in the literature. In this series, however, 5 cases (5.6 per cent.) were found. One of these is presented in detail (Case II.).

Chantemesse, Rendu, Hodenpyl, and Laveran describe single cases of ulceration of the large intestine alone. It may be mentioned here that Chantemesse[1] states that the typhoid ulcers may be absent throughout, except in the appendix, but he gives no details.

The distribution of the ulcers in typhoid fever having been elaborated in the foregoing statistics, the question naturally arises as to what determines this distribution, usually so typical and yet frequently so bizarre.

The answer has not yet been attained in its entirety. It is obvious that one important factor in determining the seat of the lesions is the extent and character of the lymphatic apparatus in the part. Yet the frequent occurrence of pharyngeal and laryngeal involvement, and the occurrence of such atypical cases as the two presented in this paper, indicate that accidental lodgement of the typhoid bacilli is another factor of considerable importance.

Moreover, the many authentic cases of typhoid fever without ulceration point to the existence of other possible factors, such as a lowered resistance of the gastrointestinal mucosa, which in these cases without ulcerations has reached its lowest ebb.

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[1] Traité de Médecine, p. 744.

In conclusion, I desire to thank Prof. L. Hektoen and Dr. H. G. Wells for much valuable advice and criticism.

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TYPHOIDAL PERFORATION:

WITH A REPORT OF EIGHT CASES SUBJECTED TO OPERATION; TWO RECOVERIES.*

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In 1884 Leyden first suggested and Mikulicz first practised suture of a perforated typhoid ulcer. In 1885 James C. Wilson brought the subject before the profession of America, and more recently (1898) interest was aroused in this subject by the brochure of Keen. That operation is still too seldom resorted to is evident when we recall that probably over 16,000 cases perish from perforation annually in the United States,[1] and that in 1903 Harte[2] was able to collect from the literature the records of only 339 cases subjected to operation.

The mortality of typhoid fever is probably about 10 per cent., and it is said that one-third of the fatalities are due to perforation of the intestine.

Perforation usually occurs during the third, fourth, or fifth week, but may happen at any stage of the disease. Males are more frequently affected than females, and the catastrophe is more liable to take place in adolescence than in infancy or old age. When the intestinal wall becomes thinned by the process of sloughing the immediate cause of perforation may be the pressure of hardened feces, straining at stool, excessive gaseous distention of the bowel, or sudden change in posture; in a number of cases ascarides have been found in the peritoneal cavity. Perforation is usually acute and followed by marked symptoms; occasionally it is chronic and the symptoms are insidious, the peritoneal cavity being protected for some time by previous adhesions.

In approaching a case for diagnosis the age, sex, previous condition of the bowels, previous presence or absence of hemorrhage, previous severity or mildness of the disease, and the period of the

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